

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Aerinaze 2.5 mg/120 mg modified-release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2.5 mg desloratadine and 120 mg pseudoephedrine sulphate.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified-release tablet.

Blue and white bilayer oval tablet with “D12” branded to blue layer.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Aerinaze is indicated in adults and adolescents 12 years and older for the symptomatic treatment of seasonal allergic rhinitis when accompanied by nasal congestion.

4.2 Posology and method of administration

Posology

The recommended dose of Aerinaze is one tablet twice a day.

The recommended dosage and the duration of treatment should not be exceeded.

The duration of treatment should be kept as short as possible and should not be continued after the symptoms have disappeared. It is advisable to limit treatment to about 10 days, as during chronic administration the activity of pseudoephedrine sulphate may diminish. After improvement of the congestive condition of the mucosae of the upper airway, treatment may be maintained with desloratadine alone, if necessary.

Elderly patients

Patients of 60 years or older are more likely to experience adverse reactions to sympathomimetic medicinal products, such as pseudoephedrine sulphate. The safety and efficacy of Aerinaze have not been established in this population, and there are insufficient data to give adequate dose recommendations. Therefore Aerinaze should be used with caution in patients above 60 years of age.

Patients with renal or hepatic impairment

The safety and efficacy of Aerinaze have not been established in patients with impaired renal or hepatic function, and there are insufficient data to give adequate dose recommendations. Aerinaze is not recommended for use in patients with impaired renal or hepatic function.

Paediatric population

The safety and efficacy of Aerinaze in children below the age of 12 years have not been established. No data are available. Aerinaze is not recommended for use in children below the age of 12 years.

Method of administration

Oral use.

The tablet may be taken with a full glass of water but must be swallowed entirely (without crushing, breaking or chewing it). The tablet may be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in section 6.1, or to adrenergic medicinal products or to loratadine.

As Aerinaze contains pseudoephedrine sulphate, it is also contraindicated in patients who are receiving monoamine oxidase (MAO) inhibitor therapy or during the 2 weeks following the stopping of such treatment.

Aerinaze is also contraindicated in patients with:

- narrow-angle glaucoma,
- urinary retention,
- cardiovascular diseases such as ischaemic heart disease, tachyarrhythmia and severe hypertension,
- hyperthyroidism,
- a history of haemorrhagic stroke or with risk factors which could increase the risk of haemorrhagic stroke. This is due to the alpha-mimetic activity of pseudoephedrine sulphate in combination with other vasoconstrictors such as bromocriptine, pergolide, lisuride, cabergoline, ergotamine, dihydroergotamine or any other decongestant medicinal product used as a nasal decongestant, either by oral route or by nasal route (phenylpropanolamine, phenylephrine, ephedrine, oxymetazoline, naphazoline...).

4.4 Special warnings and precautions for use

Cardiovascular and general effects

Patients should be informed that the treatment should be discontinued in case of hypertension, tachycardia, palpitations or cardiac arrhythmias, nausea or any other neurological sign (such as headache or increased headache).

Caution should be exercised in the following patient groups:

- Patients with cardiac arrhythmias
- Patients with hypertension
- Patients with a history of myocardial infarction, diabetes mellitus, bladder neck obstruction, or positive anamnesis of bronchospasm
- Patients receiving digitalis (see section 4.5)

Gastrointestinal and genitourinary effects

Use with caution in patients with stenosing peptic ulcer, pyloroduodenal obstruction, and obstruction of the vesical cervix.

Central nervous system effects

Caution should also be exercised in patients being treated with other sympathomimetics (see section 4.5). These include:

- decongestants
- anorexogenics or amphetamine-type psychostimulants
- antihypertensive medicinal products
- tricyclic antidepressants and other antihistamines.

Caution should be exercised in patients suffering from migraine who are currently being treated with ergot alkaloid vasoconstrictors (see section 4.5).

Convulsions

Desloratadine should be administered with caution in patients with medical or familial history of seizures, and mainly young children, being more susceptible to develop new seizures under

desloratadine treatment. Healthcare providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.

Central nervous system stimulation with convulsions or cardiovascular collapse with accompanying hypotension may be produced by sympathomimetic amines. These effects may be more likely to occur in adolescents from 12 years old, elderly patients, or in cases of overdose (see section 4.9).

Risks of abuse

Pseudoephedrine sulphate carries the risk of abuse. Increased doses may ultimately produce toxicity. Continuous use can lead to tolerance resulting in an increased risk of overdosing. Depression may follow rapid withdrawal.

Other

Perioperative acute hypertension can occur if volatile halogenated anaesthetics are used during treatment with indirect sympathomimetic agents. Therefore, if surgery is scheduled, it is preferable to discontinue treatment 24 hours before anaesthesia.

Interference with serological testing

Athletes should be informed that treatment with pseudoephedrine sulphate could lead to positive doping tests.

The administration of Aerinaze should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reaction to dermal reactivity index.

Severe skin reactions

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema or many small pustules are observed, administration of Aerinaze should be discontinued and appropriate measures taken if needed.

4.5 Interaction with other medicinal products and other forms of interaction

Aerinaze

The following combinations are not recommended:

- digitalis (see section 4.4)
- bromocriptine
- cabergoline
- lisuride, pergolide: risk of vasoconstriction and increase in blood pressure.

No interaction studies have been performed with the combination of desloratadine and pseudoephedrine sulphate.

The interaction with Aerinaze and alcohol has not been studied. However, in a clinical pharmacology trial desloratadine taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol. No significant differences were found in the psychomotor test results between desloratadine and placebo groups, whether administered alone or with alcohol. Alcohol use should be avoided during Aerinaze treatment.

Desloratadine

No clinically relevant interactions or changes in desloratadine plasma concentrations were observed in clinical trials with desloratadine in which erythromycin or ketoconazole were co-administered.

The enzyme responsible for the metabolism of desloratadine has not been identified yet, and therefore, some interactions with other medicinal products cannot be fully excluded. Desloratadine does not inhibit CYP3A4 *in vivo*, and *in vitro* studies have shown that the medicinal product does not inhibit CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

Pseudoephedrine sulphate

Antacids increase the rate of pseudoephedrine sulphate absorption, kaolin decreases it.

Sympathomimetics

Reversible and irreversible MAO inhibitor(s) may cause: risk of vasoconstriction and increased blood pressure.

Concurrent administration with other sympathomimetics (decongestants, anorexogenics or amphetamine-type psychostimulants, antihypertensive medicinal products, tricyclic antidepressants and other antihistamines) may result in critical hypertension reactions (see section 4.4).

Dihydroergotamine, ergotamine, methylergometrine: risk of vasoconstriction and increase in blood pressure.

Other vasoconstrictors used as nasal decongestant, by oral or nasal route (phenylpropanolamine, phenylephrine, ephedrine, oxymetazoline, naphazoline...): risk of vasoconstriction.

Sympathomimetic medicines reduce the antihypertensive effect of α -methyldopa, mecamylamine, reserpine, veratrum alkaloids, and guanethidine.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of the combination of desloratadine and pseudoephedrine sulphate in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Aerinaze during pregnancy.

Breast-feeding

Desloratadine and pseudoephedrine sulphate have been identified in breastfed newborns/infants of treated women. There is insufficient information on the effects of desloratadine and pseudoephedrine sulphate in newborns/infants. Decreased milk production in nursing mothers has been reported with pseudoephedrine sulphate. Aerinaze should not be used during breast-feeding.

Fertility

There are no data available on male and female fertility.

4.7 Effects on ability to drive and use machines

Aerinaze has no or negligible influence on the ability to drive and use machines. Patients should be informed that most people do not experience drowsiness. Nevertheless, as there is individual variation in response to all medicinal products, it is recommended that patients are advised not to engage in activities requiring mental alertness, such as driving a car or using machines, until they have established their own response to the medicinal product.

4.8 Undesirable effects

Summary of the safety profile

In clinical trials involving 414 adults the most frequent of adverse reactions reported were insomnia (8.9 %), dry mouth (7.2 %) and headache (3.1 %).

Tabulated list of adverse reactions

Adverse reactions considered by investigators to be causally related to Aerinaze are listed below by System Organ Class. Frequencies are defined as very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) and not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse reactions seen with Aerinaze
Metabolism and nutrition disorders	Common	Decreased appetite
	Uncommon	Thirst, glycosuria, hyperglycaemia
Psychiatric disorders	Common	Insomnia, somnolence, sleep disorder, nervousness
	Uncommon	Agitation, anxiety, irritability
Nervous system disorders	Common	Dizziness, psychomotor hyperactivity
	Uncommon	Hyperkinesia, confusional state
Eye disorders	Uncommon	Vision blurred, dry eye
Cardiac disorders	Common	Tachycardia
	Uncommon	Palpitation, supraventricular extrasystoles
Respiratory, thoracic and mediastinal disorders	Common	Pharyngitis
	Uncommon	Rhinitis, sinusitis, epistaxis, nasal discomfort, rhinorrhea, dry throat, hyposmia
Gastrointestinal disorders	Common	Constipation
	Uncommon	Dyspepsia, nausea, abdominal pain, gastroenteritis, abnormal faeces
Skin and subcutaneous tissue disorders	Uncommon	Pruritus
Renal and urinary disorders	Uncommon	Dysuria, micturition disorder
General disorders and administration site conditions	Common	Headache, fatigue, dry mouth
	Uncommon	Chills, flushing, hot flush
Investigations	Uncommon	Hepatic enzymes increased

Other adverse reactions reported for desloratadine during the post-marketing period are listed hereunder.

System Organ Class	Frequency	Adverse reactions
Immune system disorders	Very rare	Hypersensitivity (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria)
Metabolism and nutrition disorders	Not known	Increased appetite
Psychiatric disorders	Very rare	Hallucination
	Not known	Abnormal behaviour, aggression, depressed mood
Nervous system disorders	Very rare	Convulsion
Cardiac disorders	Not known	QT prolongation
Gastrointestinal disorders	Very rare	Vomiting, diarrhoea
Hepatobiliary disorders	Very rare	Hepatitis
Musculoskeletal and connective tissue disorders	Very rare	Myalgia
Investigations	Very rare	Blood bilirubin increased
	Not known	Weight increased

Cases of severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported with pseudoephedrine-containing products.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

4.9 Overdose

Symptoms

Symptoms of overdose are mostly of a sympathomimetic nature. Symptoms may vary from CNS depression (sedation, apnoea, diminished mental alertness, cyanosis, coma, cardiovascular collapse) to CNS stimulation (insomnia, hallucination, tremors, convulsions) with possible fatal outcome. Other symptoms may include: headache, anxiety, micturition difficulty, muscle weakness and tenseness, euphoria, excitement, respiratory failure, cardiac arrhythmias, tachycardia, palpitations, thirst, perspiration, nausea, vomiting, precordial pain, dizziness, tinnitus, ataxia, blurred vision and hypertension or hypotension. CNS stimulation is particularly likely in children, as are atropine-like symptoms (dry mouth, fixed and dilated pupils, flushing, hyperthermia, and gastrointestinal symptoms). Some patients may present a toxic psychosis with delusions and hallucinations.

Management

In the event of overdose, symptomatic and supportive treatment immediately should be started and maintained it for as long as necessary. Adsorption of active substance remaining in the stomach may

be attempted by administration of active charcoal suspended in water. Gastric lavage with physiologic saline solution may be performed, particularly in children. In adults, tap water can be used. As much as possible of the amount administered should be removed before the next instillation. Desloratadine is not removed by haemodialysis and it is not known if it is eliminated by peritoneal dialysis. After emergency treatment, medical monitoring of the patient should be continued.

Treatment of the pseudoephedrine sulphate overdose is symptomatic and supportive. Stimulants (analeptics) must not be used. Hypertension can be controlled with an adrenoceptor-blocking agent and tachycardia with a beta-blocking agent. Short acting barbiturates, diazepam or paraldehyde may be administered to control seizures. Hyperpyrexia, especially in children, may require treatment with tepid water sponge baths or hypothermia blanket. Apnoea is treated with respiratory assistance.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nasal preparations, nasal decongestants for systemic use, ATC code: R01BA52.

Mechanism of action

Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H₁-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H₁-receptors because the substance is excluded from entry to the central nervous system.

Desloratadine has demonstrated antiallergic properties from *in vitro* studies. These include inhibiting the release of proinflammatory cytokines such as IL-4, IL-6, IL-8, and IL-13 from human mast cells/basophils, as well as inhibition of the expression of the adhesion molecule P-selectin on endothelial cells.

Desloratadine does not readily penetrate the central nervous system. In a single dose study performed in adults, desloratadine 5 mg did not affect standard measures of flight performance including exacerbation of subjective sleepiness or tasks related to flying. In controlled clinical trials, at the recommended dose of 5 mg daily, there was no excess incidence of somnolence as compared to placebo. Desloratadine given at a single daily dose of 7.5 mg did not affect psychomotor performance in clinical trials.

Pseudoephedrine sulphate (d-isoeephedrine sulphate) is a sympathomimetic agent with mostly α -mimetic activity in comparison with the β -activity. Pseudoephedrine sulphate provides a nasal decongestant effect after oral administration due to its vasoconstrictive action. It has an indirect sympathomimetic effect due primarily to the release of adrenergic mediators from the post-ganglionic nerve endings.

Oral administration of pseudoephedrine sulphate at the recommended dose can cause other sympathomimetic effects, such as increased blood pressure, tachycardia or manifestations of central nervous system excitation.

Pharmacodynamic effects

The pharmacodynamic effects of Aerinaze tablets are directly related to that of its components.

Clinical efficacy and safety

The clinical efficacy and safety of Aerinaze tablets was evaluated in two, 2-week multicentre, randomized parallel group clinical trials involving 1,248 patients 12 to 78 years of age with seasonal allergic rhinitis, 414 of whom received Aerinaze tablets. In both trials, the antihistaminic efficacy of Aerinaze tablets as measured by total symptom score, excluding nasal congestion, was significantly greater than pseudoephedrine sulphate alone over the 2-week treatment period. In addition, the

decongestant efficacy of Aerinaze tablets, as measured by nasal stuffiness/congestion, was significantly greater than desloratadine alone over the 2-week treatment period.

There were no significant differences in the efficacy of Aerinaze tablets across subgroups of patients defined by gender, age, or race.

5.2 Pharmacokinetic properties

- Desloratadine and Pseudoephedrine sulphate:

Absorption

In a single dose pharmacokinetic study with Aerinaze, plasma concentration of desloratadine can be detected within 30 minutes of administration. The mean time to maximum plasma concentrations (T_{max}) for desloratadine occurred at approximately 4-5 hours post dose and mean peak plasma concentrations (C_{max}) and area under the concentration-time curve (AUC) of approximately 1.09 ng/ml and 31.6 ng•hr/ml, respectively, were observed. For pseudoephedrine sulphate, the mean T_{max} occurred at 6-7 hours post dose and mean peak plasma concentrations (C_{max} and AUC) of approximately 263 ng/ml and 4,588 ng•hr/ml, respectively, were observed. Food had no effect on the bioavailability (C_{max} and AUC) of desloratadine or pseudoephedrine sulphate. The half-life for desloratadine is 27.4 hours. The apparent half-life of pseudoephedrine sulphate is 7.9 hours.

Following oral administration of Aerinaze for 14 days in normal healthy volunteers, steady-state conditions were reached on day 10 for desloratadine, 3-hydroxydesloratadine and pseudoephedrine sulphate. For desloratadine, mean steady state peak plasma concentrations (C_{max} and AUC (0-12 h)) of approximately 1.7 ng/ml and 16 ng•hr/ml were observed, respectively. For pseudoephedrine sulphate, mean steady state peak plasma concentrations (C_{max} and AUC (0-12 h)) of 459 ng/ml and 4,658 ng•hr/ml were observed.

- Desloratadine

Absorption

In a series of pharmacokinetic and clinical trials, 6 % of the subjects reached a higher concentration of desloratadine. The prevalence of this poor metabolizer phenotype was greater among Black adults than Caucasian adults (18 % vs. 2 %) however the safety profile of these subjects was not different from that of the general population. In a multiple-dose pharmacokinetic study conducted with the tablet formulation in healthy adult subjects, four subjects were found to be poor metabolisers of desloratadine. These subjects had a C_{max} concentration about 3-fold higher at approximately 7 hours with a terminal phase half-life of approximately 89 hours.

Distribution

Desloratadine is moderately bound (83 % - 87 %) to plasma proteins.

- Pseudoephedrine sulphate

Absorption

A component interaction study demonstrated that the exposure (C_{max} and AUC) of pseudoephedrine sulphate following administration of pseudoephedrine sulphate alone was bioequivalent to pseudoephedrine sulphate exposure following administration of the Aerinaze tablet. Therefore absorption of pseudoephedrine sulphate was not affected by the Aerinaze formulation.

Distribution

Pseudoephedrine sulphate is presumed to cross the placenta and the haematoencephalic barrier.

The active substance is excreted in breast milk of breast-feeding women.

Elimination

Its elimination half-life in humans, at an approximate urinary pH of 6, ranges from 5 to 8 hours. The active substance and its metabolite are excreted in urine; 55-75 % of the administered dose is excreted unchanged. The rate of excretion is accelerated and the duration of action decreased in acidic urine (pH5). In case of alkalinisation of the urine, a partial resorption takes place.

5.3 Preclinical safety data

No pre-clinical studies have been performed with Aerinaze. However, non-clinical data with desloratadine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

The lack of carcinogenic potential was demonstrated in studies conducted with desloratadine and loratadine.

The combination of loratadine/pseudoephedrine sulphate used in acute and multiple-dose studies, exhibited a low order of toxicity. The combination was not more toxic than their individual components, and observed effects were generally related to the pseudoephedrine sulphate component.

During reproductive toxicity studies, the combination of loratadine/pseudoephedrine sulphate was not teratogenic when administered orally to rats at doses up to 150 mg/kg/day and rabbits at doses up to 120 mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Blue, immediate-release layer
maize starch
microcrystalline cellulose
edetate disodium
citric acid
stearic acid
colorant (Indigo carmine E132 Aluminium lake).

White, sustained-release layer
hypromellose 2208
microcrystalline cellulose
povidone K30
silicon dioxide
magnesium stearate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 30°C. Keep the blisters in the outer carton in order to protect from light.

6.5 Nature and contents of container

Aerinaze is supplied in blisters comprised of laminate blister film and foil lidding. The blister consists of clear polychlorotrifluorethylene/polyvinyl chloride (PCTFE/PVC) film, sealed with a vinyl heat seal coated aluminium foil. Pack sizes of 2, 4, 7, 10, 14 and 20 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

N.V. Organon
Kloosterstraat 6
5349 AB Oss
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/399/001
EU/1/07/399/002
EU/1/07/399/003
EU/1/07/399/004
EU/1/07/399/005
EU/1/07/399/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30 July 2007
Date of latest renewal: 30 July 2012

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

ANNEX II

- A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

SP Labo N.V.
Industriepark 30
2220 Heist-op-den-Berg
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

Not applicable.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF 2, 4, 7, 10, 14, 20 MODIFIED-RELEASE TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Aerinaze 2.5 mg/120 mg modified-release tablets
desloratadine/pseudoephedrine sulphate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 2.5 mg desloratadine and 120 mg pseudoephedrine sulphate

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

2 modified-release tablets
4 modified-release tablets
7 modified-release tablets
10 modified-release tablets
14 modified-release tablets
20 modified-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Swallow the tablet whole with water.
Do not crush, break or chew.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.
Keep the blisters in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

N.V. Organon
Kloosterstraat 6
5349 AB Oss
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/399/001 2 modified-release tablets
EU/1/07/399/002 4 modified-release tablets
EU/1/07/399/003 7 modified-release tablets
EU/1/07/399/004 10 modified-release tablets
EU/1/07/399/005 14 modified-release tablets
EU/1/07/399/006 20 modified-release tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aerinaze

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Aerinaze 2.5 mg/120 mg modified-release tablets
desloratadine/pseudoephedrine sulphate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Organon

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Aerinaze 2.5 mg/120 mg modified-release tablets desloratadine/pseudoephedrine sulphate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs or illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. **See section 4.**

What is in this leaflet:

1. What Aerinaze is and what it is used for
2. What you need to know before you take Aerinaze
3. How to take Aerinaze
4. Possible side effects
5. How to store Aerinaze
6. Contents of the pack and other information

1. What Aerinaze is and what it is used for

What Aerinaze is

Aerinaze tablets contain a combination of two active ingredients, desloratadine which is an antihistamine and pseudoephedrine sulphate which is a decongestant.

How Aerinaze works

Antihistamines help to reduce allergic symptoms by preventing the effects of a substance called histamine, which is produced by the body. Decongestants help to clear nasal congestion (blocked/stuffy nose).

When Aerinaze should be used

Aerinaze tablets relieve symptoms associated with seasonal allergic rhinitis (hay fever), such as, sneezing, runny or itchy nose, and eyes, when accompanied by nasal congestion in adults and adolescents 12 years of age and older.

2. What you need to know before you take Aerinaze

Do not take Aerinaze:

- if you are allergic to desloratadine, pseudoephedrine sulphate, adrenergic medicines, or any of the other ingredients of this medicine (listed in section 6) or to loratadine
- if you have high blood pressure, heart or blood vessel disease or a history of stroke
- if you have glaucoma, difficulty in urinating, urinary tract blockage, or an overactive thyroid
- if you are taking monoamine oxidase (MAO) inhibitor (a class of antidepressant medicines) therapy or have stopped taking these types of medicines within the last 14 days.

Warnings and precautions

Certain conditions may make you unusually sensitive to the decongestant pseudoephedrine sulphate contained in this medicine. Talk to your doctor, pharmacist or nurse before taking Aerinaze:

- if you are 60 years of age or older. Older adults may be more sensitive to the effects of this medicine
- if you have diabetes

- if you have intestinal ulcers leading to the narrowing of the stomach, small intestine or esophagus (stenosing peptic ulcer)
- if you have intestinal blockage (pyloral or duodenal blockage)
- if you have bladder neck blockage (vesical cervix blockage)
- if you have a history of difficulty breathing due to tightening of the lung muscles (bronchospasm)
- if you have problems with your liver, kidney, or bladder.

In addition, if you experience or are diagnosed with any of the following conditions you should talk to your doctor, pharmacist or nurse as they may advise you to stop taking Aerinaze:

- high blood pressure
- a fast or pounding heart beat
- abnormal heart rhythm
- feeling sick and headache or increase headache while using Aerinaze.
- if you have medical or familial history of seizures
- severe skin reactions, including signs and symptoms such as reddening of the skin, many small pimples, with or without fever

If you are scheduled to have surgery, your doctor may advise you to stop taking Aerinaze 24 hours beforehand.

One of the active ingredients in Aerinaze, pseudoephedrine sulphate, has the potential to be abused and large doses of pseudoephedrine sulphate can be toxic. Continuous use may lead to taking more Aerinaze than the recommended dose to get the desired effect, resulting in an increased risk of overdosing. If you suddenly stop treatment, depression may occur.

Laboratory tests

Stop taking Aerinaze at least 48 hours before you have any skin tests since antihistamines may influence the result of the skin test.

Athletes taking Aerinaze may have positive doping-tests.

Use in children and adolescents

Do not give this medicine to children less than 12 years of age.

Other medicines and Aerinaze

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This is especially important if you are taking:

- digitalis, a medicine used to treat certain heart disorders
- medicines for blood pressure (e.g. α -methyl dopa, mecamylamine, reserpine, veratrum alkaloids and guanethidine)
- decongestants by oral or nasal route (such as phenylpropanolamine, phenylephrine, ephedrine, oxymetazoline, naphazoline)
- diet pills (appetite suppressants)
- amphetamines
- medicines for migraines e.g. ergot alkaloids (such as, dihydroergotamine, ergotamine, or methylergometrine)
- medicines for Parkinson's disease or for infertility e.g. bromocriptine, cabergoline, lisuride and pergolide
- antacids for indigestion or stomach problems
- a medicine for diarrhoea called kaolin.
- tricyclic antidepressants (such as nortriptyline), antihistamines (such as cetirizine, fexofenadine)

Aerinaze with alcohol

Speak with your doctor, pharmacist or nurse regarding whether you can drink alcohol while taking Aerinaze. Drinking alcohol while taking Aerinaze is not recommended.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before taking this medicine.

Taking Aerinaze is not recommended if you are pregnant.

Decreased milk production in nursing mothers has been reported with pseudoephedrine sulphate, a component of Aerinaze. Desloratadine and pseudoephedrine sulphate are both excreted in human milk. If you are breast-feeding taking Aerinaze is not recommended.

Fertility

There is no data available on male/female fertility.

Driving and using machines

At the recommended dose, this medicine is not expected to affect your ability to drive or use machines. Although most people do not experience drowsiness, it is recommended not to engage in activities requiring mental alertness, such as driving a car or operating machinery until you have established your own response to the medicinal product.

3. How to take Aerinaze

Always take this medicine exactly as your doctor, pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure.

Adults and adolescents 12 years of age and over

The recommended dose is one tablet twice daily with a glass of water, with or without food.

This medicine is for oral use.

Swallow the tablet whole; do not crush, break or chew the tablet before swallowing.

Do not take more tablets than recommended on the label. Do not take tablets more often than recommended.

Do not take this medicine for more than 10 days continuously unless your doctor tells you to do so.

If you take more Aerinaze than you should

If you take more Aerinaze than you were told to, tell your doctor, pharmacist or nurse immediately.

If you forget to take Aerinaze

If you forget to take your dose on time, take it as soon as possible and then go back to your regular dosing schedule. Do not take a double dose to make up for a forgotten dose.

If you stop taking Aerinaze

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects have been seen in studies:

Common: the following may affect up to 1 in 10 people

- fast heartbeat
- decreased appetite
- tiredness
- restlessness with increased body movement
- constipation
- headache
- dry mouth
- trouble sleeping
- dizziness
- nervousness
- sore throat
- drowsiness

Uncommon: the following may affect up to 1 in 100 people

- pounding or irregular heart beat
- dry throat
- itching
- increased body movement
- stomach ache
- chills
- flushing
- stomach flu
- decreased sense of smell
- hot flush
- feeling sick (nausea)
- abnormal liver function tests
- confusion
- abnormal stool
- agitation
- blurry vision
- painful or difficult urination
- anxiety
- dry eye
- sugar in urine
- irritability
- nose bleeds
- increased sugar in blood
- irritated nose
- thirst
- inflammation of the nose
- problems urinating
- runny nose
- changes in frequency of urination
- inflammation of the sinus
- urination

Very rarely: the following other side effects reported during the marketing of desloratadine, may affect up to 1 in 10,000 people

- severe allergic reactions (difficulty in breathing, wheezing, itching, hives and swelling)
- vomiting
- muscle pain
- rash
- diarrhoea
- convulsion
- hallucination
- liver inflammation
- abnormal liver function tests

Not known: frequency cannot be estimated from the available data

- abnormal behaviour
- aggression
- changes in the way the heart beats
- weight increased, increased appetite
- depressed mood

Cases of severe skin reactions, including signs and symptoms such as fever, reddening of the skin, or many small pimples, have been reported with pseudoephedrine-containing products.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aerinaze

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer carton and blister after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C. Keep the blisters in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Aerinaze contains

- The active substances are desloratadine and pseudoephedrine sulphate.
- Each tablet contains 2.5 mg desloratadine and 120 mg pseudoephedrine sulphate.
- The other ingredients are:
 - *Ingredients in the blue, immediate-release layer:* maize starch, microcrystalline cellulose, edetate disodium, citric acid, stearic acid and colorant (Indigo Carmine E132, Aluminum lake).
 - *Ingredients in the white, sustained-release layer:* hypromellose 2208, microcrystalline cellulose, povidone K30, silicon dioxide and magnesium stearate.

What Aerinaze looks like and contents of the pack

Aerinaze is a blue and white oval bilayer modified-release tablet with “D12” debossed in the blue layer. Aerinaze tablets are packed as 2, 4, 7, 10, 14, or 20 tablets in blisters comprised of laminate blister film and foil lidding.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

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The Netherlands

Manufacturer:

SP Labo N.V.
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.

ANNEX IV

**SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE VARIATION TO THE TERMS
OF THE MARKETING AUTHORISATION(S)**

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for desloratadine / pseudoephedrine, the scientific conclusions of the CHMP are as follows:

In view of available data from the literature including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between desloratadine and depressed mood is at least a reasonable possibility. The PRAC concluded that the product information (PI) of products containing desloratadine / pseudoephedrine should be amended accordingly.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for desloratadine / pseudoephedrine the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing desloratadine / pseudoephedrine is unchanged subject to the proposed changes to the product information.

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.